

IS FATTY ACID METABOLISM ALTERED IN ADRIAMYCIN CARDIOMYOPATHY?

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To determine whether fatty acid metabolism is altered in adriamycin cardiomyopathy, and to identify the associated cellular site, we measured palmitate (PA) oxidation kinetics and incorporation into the neutral lipid pool (NLP) in a rat model of ACM (n=22) compared to normals (CTL, n=13). In an isolated heart preparation, 1.2mM/L of 14 C-PA was perfused for 30 min to achieve steady state oxidation, measured as 14 CO₂ production at 1, 10, 20 and 30 min of the 14 C-PA perfusion. Hearts were sacrificed < 5 min (E) or 10-30 min (L) after the 14 C-PA perfusion to measure 14 C-PA incorporation into NLP, and NLP utilization. The results are as follows (mean±SEM, *p<0.01, #p<0.05):

	14 CO ₂ production (nM/min/g dry wt)		14 C-PA incorporation into NLP (μM/g dry wt)	
	10 min	30 min	E	L
CTL	580±61*	617±36	12.03±1.36*#	8.70±0.9#
ACM	329±65*#	521±65#	7.22±0.63*	8.65±0.9

Thus in adriamycin cardiomyopathy, there is (1) significant delay in achieving steady state oxidation, although the steady state rate is near normal; (2) reduced fatty acid incorporation into the neutral lipid pool; (3) reduced neutral lipid pool utilization. This suggests impairment of cell membrane and possibly mitochondrial membrane fatty acid uptake in adriamycin cardiomyopathy, with relatively maintained capacity for oxidative metabolism.

EFFECT OF RAPID VENTRICULAR PACING ON INTRACELLULAR SODIUM IN ISOLATED PERFUSED RAT HEARTS

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The concentration of intracellular sodium, ([Na⁺]_i), is thought to play a critical role in regulation of contractile state via sodium-calcium exchange. Although rat myocardium has not been shown to exhibit a positive inotropic response to increased heart rate (positive staircase), recent ²³Na nuclear magnetic resonance studies using dysprosium tripolyphosphate as the shift agent have suggested that pacing increases both [Na⁺]_i and developed pressure. A newly developed shift agent, thulium 1,4,7,10-tetraazacyclododecane-N,N',N'',N'''-tetra(methylenephosphonate) (Tm(DOTP)³⁻), was used to measure [Na⁺]_i in isolated rat hearts using ²³Na spectroscopy at 11.74 Tesla; free calcium concentration was physiological (1.0 mM). Isovolumic pressures were measured with a Millar transducer connected to the intraventricular balloon. Hearts were studied at native heart rates and then paced at 300, 400 and 500 beats per minute. With increasing heart rate, developed pressure decreased to 50% of control at maximum paced heart rate and [Na⁺]_i did not change. The differences between this study and earlier reports are attributed to the use of Tm(DOTP)³⁻ which is chemically stable and allows physiological free calcium concentrations in the perfusing medium.

REGIONAL MYOCARDIAL PERFUSION AND GLUCOSE METABOLISM IN LEFT BUNDLE BRANCH BLOCK (LBBB)

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To evaluate the mechanism of false positive Tl-201 tomography (SPECT) in LBBB, we studied four patients with Tl-SPECT and F-18 deoxyglucose (FDG) positron tomography. Both images showed septal defects and echocardiographic examination revealed impaired systolic thickening in the septum.

To elucidate the mechanism, we induced LBBB pattern with right ventricular pacing in open chest dogs (n=12) and examined myocardial uptake of Tl and FDG, systolic thickening and intramyocardial pressure (IMP) in the septum. Septal uptake of Tl and FDG was decreased significantly compared with the free wall (74.7±14.5% vs 86.5±5.3% and 67.4±12.1% vs 88.0±5.2% : P<0.05). Septal thickening was also reduced (0.98±0.05 vs 1.35±0.15 : P<0.05) with augmented IMP in diastolic phase. But aortic pressure and flow of left anterior descending coronary artery showed no change, and lactate production was not detected.

Thus false positive Tl-SPECT in LBBB appears to imply decreased myocardial perfusion and glucose metabolism in the septum due to impaired systolic thickening with increased IMP in diastolic phase, and not ischemia.

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Poster Displayed: 2:00PM-5:00PM

Author Present: 3:00PM-4:00PM

Hall F, West Concourse

Ventricular Arrhythmias and Sudden Death

SYNCOPE: A WARNING SIGN OF SUDDEN DEATH IN IDIOPATHIC DILATED CARDIOMYOPATHY PATIENTS

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Identification of dilated cardiomyopathy (DCM) patients (pts) at high risk for sudden cardiac death (SCD) is useful in providing preventive therapy. We analyzed the outcome of 48 DCM pts who did not have clinically documented sustained ventricular tachyarrhythmias. Pts were grouped by mode of presentation. Group 1 presented with syncope. Group 2 presented with dizziness or lesser symptoms. All pts underwent electrophysiology study (EPS). Antiarrhythmic drug therapy was guided by EPS results. No patients received an implantable defibrillator. Clinical variables and follow-up durations were similar in both groups. Outcomes are as follows:

Group #	1 (N=16)		2 (N=34)	
EPS result	SMVT	NEG	SMVT	NEG
N=	3	13	4	30
SCD	1	5	0	1
Other deaths	2	0	2	6
4 Yr survival:				
SCD/all deaths	.44/.38		.96/.74	

Incidence of SCD was higher in Group 1 (p<0.05).

Conclusions: DCM Pts presenting with syncope are at high risk for sudden death. Results of EPS were not useful in this group as they remained at high risk for SCD despite negative EPS. Implanted defibrillators may be the only effective therapy for Group 1 pts.